WE CLAIM:

1. A method of identifying redundant clones in a cDNA library comprising:

(a) identifying at least one redundant clone in a first portion of the cDNA library;

(b) obtaining an isolated polynucleotide corresponding to said redundant clone;

(c) hybridizing a detectably labeled probe to an array of clones from the cDNA library, wherein said hybridizing is done in the presence and absence of the isolated polynucleotide obtained in (b);

(d) comparing the hybridization signal obtained for each arrayed clone in the presence and absence of the isolated polynucleotide; and,

(e) identifying clones for which the hybridization signal produced is different in the presence and absence of the isolated polynucleotide as redundant clones.

2. The method of claim 1 wherein the redundant clone is identified by comparing the sequences of at least 100 clones in said first portion of the cDNA library.

3. The method of claim 1 wherein the isolated polynucleotide in (d) is unlabeled.

4. The method of claim 1 wherein the isolated polynucleotide in (d) is detectably labeled.

5. A method of identifying previously characterized clones in a cDNA library comprising

(a) obtaining an isolated polynucleotide corresponding to previously identified clones;

(b) hybridizing a detectably labeled probe to an array of clones from the cDNA library in the presence and absence of the isolated polynucleotide obtained in (a);

(d) comparing the hybridization signal obtained for each arrayed clone in the presence and absence of the isolated polynucleotide; and,

(e) identifying clones for which the hybridization signal produced is different in the presence and absence of the isolated polynucleotide as previously characterized clones.

6. An improved method of making a normalized or subtracted cDNA library comprising:

(a) obtaining double-stranded cDNA (dscDNA) corresponding to mRNA from a tissue or cell;

(b) restricting a first portion of said dscDNA with a first restriction enzyme;

(c) restricting a second portion of said dscDNA with a second restriction enzyme, wherein

(i) restriction of dscDNA from the tissue or cell with the first enzyme s predicted to produce restriction fragments having a predicted average fragment size of between about 100 and about 500 basepairs;

(ii) restriction of dscDNA from the tissue or cell with the second enzyme is predicted to produce restriction fragments having a predicted average fragment size of between about 100 and about 500 basepairs; and,

(iii) the predicted average fragment size in (i) and (ii) are within about 150 basepairs of each other; and,

(d) combining said first and second portions.

7. The method of claim 6 wherein the predicted average fragment sizes in (i) and (ii) is between 300 and 500 basepairs.

8. The method of claim 7 wherein the predicted average fragment sizes in (i) and (ii) are within about 100 basepairs of each other.

9. The method of claim 6 wherein the tissue or cell is from a mammal.

10. The method of claim 9 wherein the animal is rat, mouse, human or non-human primate.

11. The method of claim 10 wherein at least one of the first and second enzymes is selected from the group consisting of Alu I, Cvi RI, Dpn I, Hae III, Rsa I, Cvi J1 and Tha 1.

12. The method of claim 10 where the first enzyme is Dpn 1 and the second enzyme is Rsa 1.

13. The method of claim 6 wherein the predicted average fragment size is determined by inspection of gene sequences from Genbank.

14. The method of claim 13 wherein the inspection is computer implemented.

15. A method for selecting clones for analysis comprising:

(a) preparing double-stranded cDNA (dscDNA) corresponding to mRNA from each of a pair of related tissues or cells, wherein one member of the pair is designated the driver-tissue and the other member of the pair is designated the tester-tissue;

(b) using said dscDNA to prepare a driver-normalized cDNA library, a tester-normalized cDNA library, a driver-subtracted cDNA library, and a tester-subtracted cDNA library;

(c) hybridizing clones from each of the libraries in (b) with detectably labeled cDNA probe corresponding to mRNA from one or both of the related tissues or cells;

(d) selecting clones with a desired signal intensity from the driver-normalized cDNA library hybridized with cDNA probe from the driver tissue and the tester-normalized cDNA library hybridized with cDNA probe from the tester tissue; and,

(e) selecting clones with a desired ratio of hybridization signal from the driver-subtracted cDNA library hybridized with cDNA probe corresponding to mRNA from both of the related tissues and the tester-subtracted cDNA library hybridized with cDNA probe corresponding to mRNA from both of the related tissues.

16. The method of claim 15 wherein the tissues are from rat, mouse, human or non-human primate.

17. The method of claim 15 wherein the mRNA is from a pair of tissues related as diseased tissue and healthy tissue.

18. The method of claim 17 wherein the diseased tissue is from brain.

19. The method of claim 15 wherein the diseased tissue is from an animal model of a human disease.

20. A method for selecting clones for analysis comprising:

(a) preparing double-stranded cDNA (dscDNA) corresponding to mRNA from each of a pair of related tissues or cells, wherein one member of the pair is designated the driver-tissue and the other member of the pair is designated the tester-tissue;

(b) using said dscDNA to prepare a driver-normalized cDNA library, a tester-normalized cDNA library, a driver-subtracted cDNA library, and a tester-subtracted cDNA library;

(c) hybridizing clones from each of the libraries in (b) with detectably labeled cDNA probe corresponding to mRNA from one or both of the related tissues or cells;

(d) selecting low signal clones from the driver-normalized cDNA library hybridized with cDNA probe from the driver tissue;

(e) selecting low signal clones from the tester-normalized cDNA library hybridized with cDNA probe from the tester tissue;

(f) selecting high-ratio clones from the driver-subtracted cDNA library hybridized with cDNA probe corresponding to mRNA from both of the related tissues; and,

(g) selecting high-ratio clones from the tester-subtracted cDNA library hybridized with cDNA probe corresponding to mRNA from both of the related tissues.

21. A method for comparing the quality of a two different subtracted cDNA libraries, comprising:

(a) obtaining a first subtracted cDNA library and a second subtracted cDNA library, wherein each library is prepared from the same tester and driver RNAs;

(b) preparing detectably labeled probe from DNA from each library;

(c) hybridizing said probe from each library to an array of immobilized polynucleotides, wherein at least a plurality of said polynucleotides have the sequence of genes that are differentially expressed in the tester RNA compared to the driver RNA, and detecting the hybridization of the probe to the immobilized polynucleotides;

(d) identifying at least one immobilized polynucleotide having a sequence that is differentially expressed in the tester RNA compared to the driver RNA and comparing the level of hybridization of probe from the first subtracted cDNA library to said polynucleotide with the level of hybridization of probe from the second subtracted cDNA library to said polynucleotide,

wherein, the library having the higher level of hybridization of probe to said polynucleotide is identified as a higher quality library.